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„Activities of daily living in the early detection of dementia concerning patients with Subjective cognitive decline, Mild cognitive impairment and Parkinson’s disease.“

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Diploma Thesis

Activities of daily living in the early detection of dementia concerning patients with Subjective cognitive decline, Mild cognitive impairment and Parkinson's disease.

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## **Abstract**

**Background:** Restrictions in activities of daily living (ADL) are assumed to be associated with early cognitive decline and therefore could contribute to better prognostication of Alzheimer's disease (AD) and Parkinson disease dementia (PDD).

**Objectives:** To investigate the meaningfulness of ADL impairment in detecting AD and PDD in patients with subjective cognitive decline (SCD) and mild cognitive impairment (MCI).

**Design:** Longitudinal study with one follow up examination.

**Methods:** Subjects who came to a memory outpatient clinic (N = 168), aged 50 and older, for clarification of a possible cognitive decline were investigated. The test procedure includes a screening, the Vienna Neuropsychological Test Battery (NTBV) and self-assessment questionnaires such as the Bayer Activities of Daily Living Scale (B-ADL).

**Results:** Subjects with MCI, especially with amnesic MCI (aMCI) reported more restrictions in their ADL ( $p < .05$ ) and the deterioration over the study period ( $p < .01$ ) was twice as high as in those with SCD. Further, Converters to AD described more restrictions ( $p < .05$ ) and deteriorated nearly twice as high over the course of study as Non-Converters. Finally, individuals who deteriorated regarding to their diagnoses over the course of study reported poorer ADL at baseline ( $p < .05$ ) and described a greater deterioration over the course ( $p < .01$ ) compared to those who remained stable. In addition, concerning patients with Parkinson disease (PD) there were no significant outcomes.

**Conclusion:** Functional disability represents an important risk factor of cognitive decline and progression to AD. However, further research is needed to encompass the multi-system of functional impairment and its impact on cognitive decline. Concerning patients with PD no conclusions about the clinical value of functional disability in detecting PDD can be drawn based on the data of the present study.

**Keywords:** Activities of daily living, subjective cognitive decline, mild cognitive impairment, Alzheimer's disease, Parkinson's disease dementia.

## **Abstract (Deutsch)**

**Hintergrund:** Es wird angenommen, dass Einschränkungen in den Aktivitäten des täglichen Lebens (ADL) mit frühzeitigen kognitiven Einbußen einhergehen und diese aufgrund dessen einen wesentlichen Beitrag zur Prognose von Alzheimerdemenz (AD) und Parkinsondemenz (PDD) leisten könnten.

**Ziele:** Untersuchung der Bedeutsamkeit von Beeinträchtigungen in ADL hinsichtlich der frühzeitigen Erkennung von AD und PDD in Personen mit subjektiven kognitiven Abbau (SCD) und leichten kognitiven Beeinträchtigungen (MCI).

**Design:** Längsschnittstudie mit einer follow-up-Untersuchung.

**Methoden:** Untersucht wurden N = 168 Personen im Alter von zumindest 50 Jahren, welche zur Abklärung eines möglichen kognitiven Abbaus eine Gedächtnisambulanz aufsuchten. Die Datenerhebung inkludierte ein Screening, die Vienna Neuropsychological Test Battery (NTBV) und Fragebögen zur Selbstbeurteilung wie beispielsweise die Bayer Activities of Daily Living Skala (B-ADL).

**Ergebnisse:** Personen mit MCI, speziell jene mit leichten amnestischen kognitiven Beeinträchtigungen (aMCI), schilderten mehr Einschränkungen in ihren ADL ( $p < .05$ ) und die Verschlechterung über den Verlauf der Studie ( $p < .01$ ) war doppelt so hoch im Vergleich zu jenen mit SCD. Des Weiteren äußerten Personen, welche zu AD konvertierten, massivere Einschränkungen ( $p < .05$ ) und deren ADL verschlechterten sich über den Zeitraum der Studie beinahe in einem zweifach so hohen Ausmaß. Schließlich gaben Personen, die sich im Verlauf der Studie hinsichtlich ihrer Diagnosen verschlechterten, schwerwiegendere Einschränkungen zu Beginn der Studie in ihren ADL an ( $p < .05$ ) und schilderten weiters eine deutlichere Verschlechterung über den Zeitraum der Studie ( $p < .01$ ) im Vergleich zu jenen, die hinsichtlich ihrer Diagnose unverändert blieben. Darüber hinaus gab es in Bezug auf Personen, welche an einer Parkinsonerkrankung (PD) litten, keine signifikanten Ergebnisse.

**Konklusion:** Funktionale Beeinträchtigung stellt einen wesentlichen Risikofaktor für den Abbau kognitiver Fähigkeiten und den Übergang zu AD dar. Um jedoch den multidimensionalen Charakter hinsichtlich funktionaler Beeinträchtigungen und deren Einfluss auf den Abbau kognitiver Fähigkeiten gänzlich zu verstehen, benötigt es weitere Forschungsaktivitäten. In Bezug auf Patienten mit PD können aufgrund der vorliegenden Daten keine Schlussfolgerungen über deren praktische Relevanz hinsichtlich der frühzeitigen Erkennung einer möglichen PDD getroffen werden.

**Schlüsselwörter:** Aktivitäten des täglichen Lebens, subjektive kognitive Verschlechterung, leichte kognitive Beeinträchtigung, Alzheimerdemenz, Parkinsondemenz.

## 1. Introduction

### 1.1. Dementia

Dementia is a common syndrome in older people that causes severe changes in the brain, loss of mental abilities and sustainable complications in daily living (Förstl & Lang, 2011). In Austria the number of individuals with dementia is approaching 100,000. Moreover, the incidence of dementia seems to be increasing. By 2050, the number of individuals with dementia in Austria will rise to 250,000 due to the demographic changes (Gleichweit & Rossa, 2009). According to Ferri et al. (2006), it is estimated that worldwide there will be 24,3 million people living with dementia and that this number will almost double every 20 years. Thus, in 2040 there will be approximately 81 million people who will be suffering from dementia. Prince (1997) and Wimo, Winblad, Aguero-Torres and vonStrauss (2004) report comparable estimates. Furthermore, Alzheimer's disease (AD) is the most frequent reason of dementia accounting for 60% to 80% of all dementia cases and as many as 5.1 million Americans may currently be suffering from AD. Amongst other things AD is accompanied by memory loss which interferes with activities of daily living, as also difficulties in planning and solving problems, as well as difficulties in understanding visual images and spatial

relationships. Patients also show decreased judgment, changes in mood and personality and in later stages experience problems with orientation, speaking, swallowing, and walking (Alzheimer's Association, 2011; Daviglus et al., 2010).

In addition, Parkinson's disease (PD) as the second most common neurodegenerative disease can be assumed as a further cause for the occurrence of cognitive decline and dementia (Hely, Reid, Adena, Halliday & Morris, 2008). PD, with a prevalence of 1-2% in the population over 65 years, is characterized by cardinal motor features and non- motor symptoms such as bradykinesia, tremor, rigidity, automatic dysfunction, neuropsychiatric symptoms and sleep disturbances (Alves, Forsaa, Pedersen, Gjerstad & Larsen, 2008; Aarsland, Zaccai & Brayne, 2005; Gelb, Oliver & Gilman, 1999). According to the literature (Aarsland & Kurz, 2010; Aarsland et al., 2005; Cummings, 1988) the point prevalence of dementia in PD is approximately 30-40%. Furthermore, the cumulative incidence of Parkinson's disease dementia (PDD) is approaching 80%, with an annual incidence of 10% (Aarsland & Kurz, 2010; de Lau, Schipper, Hofman, Koudstaal & Breteler, 2005; Hely et al., 2008).

Moreover, AD and PDD represent a great burden for both the affected

individuals as also their relatives, who often take on a large part of care (Aarsland et al., 2007a; Alzheimer's Association, 2011; Daviglus et al., 2010; Desai, Grossberg & Sheth, 2004; Ferri et al., 2006). Additionally, the development of AD and PDD predict increased mortality (Alzheimer's Association, 2011; Levy et al., 2002). Disease-related costs incurred both at the national as well as at the individual level should also not be overlooked (Alzheimer's Association, 2011; Desai et al., 2004; Emre, 2003; Vossius, Larsen, Janvin & Aarsland, 2011). Therefore dementia constitutes a major public health concern and an important area of investigation (Ballard et al., 2011; Fauth et al., 2013).

The great objective would be to delay the onset of disease preferably until after the person's death. This could be possible if useful interventions were utilized right after the first incipient cognitive deterioration, usually reported 10 years prior to the diagnosis of dementia (Alzheimer's Association, 2011; Elias et al., 2000; Snowden et al., 1996). But according to Alzheimer's Association (2011) and Hulette et al. (1998) current treatments are applied too late, namely, when neuropathological changes have already appeared and/or do not yet consider the multiple factors, which are most likely involved in the development of

AD and PDD (Ballard et al., 2011; Daviglus et al., 2010; Docherty & Burn, 2010; Hely et al., 2008). Therefore an earlier detection of a possible incipient dementia and also an analysis of potential risk factors and precursors is inevitable. Thus, to be able to detect a possible dementia early on and to develop appropriate interventions and/or medications it must be discovered which factors actually precede an incipient dementia. Moreover it is also important to exclude those factors, which are accompanied by the cognitive degradation processes or may even be caused by these. According to current literature numerous potential risk factors such as disability in activities of daily living (ADL) (Barberger-Gateau, Dartigues & Letenneur, 1993; Di Carlo et al., 2007; Fauth et al., 2013; Luck et al., 2011; Peres et al., 2006; Reppermund et al., 2013; Sikkes et al., 2011; Tabert et al., 2002) or the precursor's subjective cognitive decline (SCD) (Blackburn et al., 2014; Dufouil, Fuhrer & Alépovitch, 2005; Geerlings, Jonker, Bouter, Adèr & Schmand, 1999; Glodzik-Sobanska et al., 2007; Jonker, Geerlings & Schmand, 2000; Jessen et al., 2010; Jessen et al., 2014; Luck et al., 2015; Reid & MacLulich, 2006; Reisberg, Shulman, Torossian, Leng & Zhu, 2010; Rönnlund, Sundström, Adolfsson & Nilsson, 2015; Schmand, Jonker, Geerlings

& Lindeboom, 1997; van Oijen, de Jong, Hofman, Koudstaal & Breteler, 2007) and mild cognitive impairment (MCI) (Forlenza, Diniz, Stella, Teixeira & Gattaz, 2013; Yarnall, Rochester & Burn, 2013) have already been detected concerning AD and PDD. (Aarsland & Kurz, 2010; Chen, Lin & Chen, 2009; Daviglus et al., 2010; Emre et al., 2007; McCullagh, Craig, McIlroy & Passmore, 2001)

## **1.2. Prodromal phases of dementia**

It is assumed that precursors exist prior to entering an incipient dementia and that these signs represent an increased risk of developing dementia. Thus, the course of the disease can be represented as following. It starts with healthy aging. Then the persons may complain about memory problems, albeit objective signs of cognitive decline are absent. This is called subjective cognitive decline (SCD). Thereafter, when memory problems or a decline in other domains like executive functions or use of language are not only subjectively evident and are severe enough a diagnosis of mild cognitive impairment (MCI) might be made. And finally, if the (objective) memory impairment gets worse it then may lead to dementia (Jessen et al., 2010).

### **1.2.1 Subjective cognitive decline (SCD) and Mild cognitive impairment (MCI)**

After the initial description of persons concerned about their memory in 1982 (Reisberg, Ferris, de Leon & Crook, 1982) this term (SCD) was conceptualized in many ways like subjective memory impairment or memory complaints, but a common definition and/or core criteria were not agreed upon (Abdulrab & Heun, 2008). Consequently, the Subjective Cognitive Decline Initiative (SCD-I) yielded a common concept and also research procedures. Thus, SCD is characterized by self-experienced decline of cognitive function, not related to other causes like an acute event, a psychiatric or neurological disease, a medication disorder or substance abuse, by normal age-, gender-, and education-adjusted performance on standardized cognitive test and absence of a diagnose such as MCI, prodromal AD or dementia (Jessen et al., 2014).

Furthermore, the term MCI emerged in the 1990s, constitutes an intermediate state between normal aging and dementia and is accompanied by subjective memory complaints, preferably corroborated by an informant, essentially (largely) intact abilities to perform activities of daily living (ADL), relatively preserved global cognition and a decline in cognition beyond that associated with typical aging, but without fulfilling the criteria of dementia. Moreover, MCI is classified into

two subtypes called non-amnesic mild cognitive impairment (naMCI) and amnesic mild cognitive impairment (aMCI). Whereas in naMCI the persons concerned show a decline in one or more domains like attention or use of language but without memory impairment itself, aMCI is characterized by memory decline and possibly also by decline in one or more other domains (Petersen et al., 1999, Petersen, 2004).

In addition, MCI among PD, called PD-MCI may also represent a pre-dementia state and its diagnostic criteria by the Movement Disorder Society Task Force are similar to that of MCI as described below (Litvan et al., 2012; Vossius et al., 2011). Further, referring to MCI and PD-MCI several longitudinal studies and systematic reviews from Forlenza et al. (2013) and Yarnall et al. (2013) emphasizes an increased risk for the development of AD and PDD (Broeders et al., 2013; Bruscoli & Lovestone, 2004; Busse, Hensel, Gühne, Angermeyer & Riedel-Heller, 2006; Hobson & Meara, 2015; Janvin, Larsen, Aarsland & Hugdahl, 2006; Lopez et al., 2003; Mitchell & Shiri-Feshki, 2009). In particular, whereas aMCI occurs more often and show a higher risk of progression to AD, (Busse et al., 2006; Luck et al., 2011; Palmer, Bäckman, Winblad & Fratiglioni, 2008; Petersen, 2011) PD-

aMCI is less common than PD-naMCI, although PD-aMCI is associated with an earlier development of PDD (Goldman & Litvan, 2011; Janvin et al., 2006).

The estimated prevalence of MCI in population-based studies ranges from 10 to 20% with a 2:1 ratio of aMCI to naMCI (Busse et al., 2006; Di Carlo et al., 2007; Lopez et al., 2003; Manly et al., 2008; Mariani, Monastero & Mecocci, 2007; Petersen, 2011; Petersen et al., 2009; Plassman et al., 2008; Roberts et al., 2008). In PD patients the estimated prevalence is even higher with 21 to 37% whereas PD-naMCI is more prevalent than PD-aMCI (Aarsland et al., 2010; Broeders et al., 2013; Dalrymple-Alford et al., 2011; Hobson & Meara, 2015; Litvan et al., 2011). Furthermore according to longitudinal studies conversion rates from MCI to dementia, particularly AD, in clinic-based studies and with regard to the Mayo criteria are 10 to 15% or rather approximately 10% per year (Brodaty, Connors, Ames & Woodward, 2014; Farias et al., 2009; Hedman, Nygård, Almkvist & Kottorp, 2013; Petersen et al., 1999; Sikkes et al., 2011). These findings are in line with the reviews from Bruscoli and Lovestone (2004) and Mitchell and Shiri-Feshki (2009). The latter indicates an annual conversion rate (ACR) of 9.6% for all forms of dementia and an ACR of 8.1% especially for AD in specialist clinical



settings. Regarding to community studies or studies not using the Mayo Criteria the ACR is about 5%. Moreover the conversion rate to dementia is almost twice as high in subjects with aMCI as in subjects with naMCI (Busse et al., 2006; Fischer et al., 2007; Luck et al., 2011; Mitchell & Shiri-Feshki, 2009).

To date, longitudinal studies concerning PD-MCI are rare (Yarnall et al., 2013). One study published an incidence of PDD in PD-MCI patients of 62% within 4 years (Janvin et al., 2006). Further, Broeders and colleagues (2013) found that only 26% of PD-MCI subjects developed PDD within 5 years. But they argued that their sample was younger and showed mild disease severity. In addition, current studies from Hobson and Meara (2015) and Lee et al. (2013) report an ACR of around 11% to 14%. Furthermore, also PD-aMCI has a stronger tendency to develop PDD than PD-naMCI (Barone et al., 2011; Tröster, 2011). But overall both prevalence rates as well as conversion rates to AD and PDD varied widely across different studies depending on the applied MCI criteria, the neuropsychological assessment and the study population (Brodaty et al., 2013; Bruscoli & Lovestone, 2004; Mitchell & Shiri-Feshki, 2009; Yarnall et al., 2013).

Beyond, however, it is assumed that subjects seeking help for memory

problems have the highest conversion rate and are therefore at high risk of developing dementia. Thus, SCD may contribute to the higher conversion rates regarding to clinic-based studies (Bruscoli & Lovestone, 2004; Jessen et al., 2010; Jonker et al., 2000). Several longitudinal cohort studies identified SCD as a pre-MCI state and risk factor of cognitive decline and future dementia, perhaps especially for those who are concerned about their memory (Blackburn et al., 2014; Dufouil et al., 2005; Geerlings et al., 1999; Glodzik-Sobanska et al., 2007; Jessen et al., 2014; Jessen et al., 2010; Jonker et al., 2000; Luck et al., 2015; Reid & MacLullich, 2006; Reisberg et al., 2010; Rönnlund et al., 2015; Schmand et al., 1997; van Oijen et al., 2007). According to the review from Mendonca, Alves and Bugalho (2015) especially subjects who describe impact of their complaints on activities of daily living, are worried about their memory and by whom informants confirmed their complaints are at higher risk of progression. Furthermore, Jessen and colleagues (2010) suggest that individuals with SCD at baseline and aMCI at follow-up are at greatest risk for conversion to dementia. Moreover, the estimated prevalence of SCD ranges from 11% to as high as 60% (Dik et al., 2001; Holmen et al., 2013; Jonker et al., 2000; Jorm, Christensen, Korten, Jacomb & Henderson,

2001; Jungwirth et al., 2004; Paradise, Glozier, Naismith, Davenport & Hickie, 2011; Singh-Manoux et al., 2014; Waldorff, Siersma, Vogel & Waldemar, 2012) and according to Jessen et al. (2010) 10% of persons with SCD convert to MCI within 3 years.

Further, SCD in PD (PD-SCD) with an estimated prevalence of approximately 25% (Erro et al., 2014) also seem to be a pre-PD-MCI state and a risk factor of cognitive decline and future PDD (Erro et al., 2014; Hong et al., 2014). Contrary to studies suggesting SCD is more related to factors such as depression and anxiety rather than cognition (Hänninen et al., 1994; Jorm et al., 1994; Jungwirth et al., 2004; Minett, Dean, Firbank, English & O'Brien, 2005), current studies found that SCD and PD-SCD are significant independent predictors for dementia and PDD regardless of the presence of depression, age, age at onset and motor disability (Erro et al., 2014; Hong et al., 2014; Schmand, Jonker, Hooijer & Lindeboom, 1996; Waldorff et al., 2012). In addition, the concept of SCD might only be useful in subjects without cognitive decline because according to Jungwirth et al. (2004) about only 6% of memory – impaired subjects expressed memory problems. Moreover, Geerlings et al. (1999) found that memory complaints were only associated with incipient AD in

subjects with normal baseline cognition but not with those who are objectively impaired. Furthermore, in PD the relationship between subjective complaints and objective cognitive performance is also accompanied by conflicting results across different studies (Dujardin et al., 2010; Koerts et al., 2012; Koerts et al., 2011). Possibly anosognosia, which is a common feature in dementia (Vogel et al., 2004), plays a role as soon as a cognitive decline occurs.

SCD and MCI as well as PD-SCD and PD-MCI seem to be important risk factors of incipient AD and PDD. But despite the supposed evidence of clinical usefulness controversy also persists with regard to these diagnostic concepts (Copeland & Schiess, 2013; Hong et al., 2014; Jessen et al., 2014; Mitchell & Shiri-Feshki, 2009; Petersen et al., 2009; Stewart, 2011). Further, it is assumed that multiple factors contribute to the genesis of AD and PDD (Aarsland & Kurz, 2010; Chen et al., 2009; Daviglus et al., 2010; Emre et al., 2007; McCullagh et al., 2001). Thus, other possible risk factors must also be taken into account to ensure early treatments and medications to deal with this public health concern.

### **1.3. Activities of daily living (ADL)**

Impairments in activities of daily living (ADL) also seem to be an important predominant feature of AD and PDD

(American Psychiatric Association, 1994; Barberger-Gateau, Fabrigoule, Rouch, Letenneur & Dartigues, 1999; Fitz & Teri, 1994; Hamer & Chida, 2009; Shulman et al., 2006; Small et al., 1997). By definition ADL disability means the difficulty to perform activities in any domain of life owing to a health or physical problem and appears when a person's capabilities do not meet the requirements of the physical and/or social environment (Verbrugge & Jette, 1994). Further ADL can be divided into three groups on the basis of difficulty and complexity. Basic activities of daily living (b-ADL/BADL) include basic physiological and self-maintenance needs like eating or toileting. Instrumental activities of daily living (i-ADL/IADL, e.g. preparing meals) describe more complex activities and ensure combined with b-ADL independent living. Finally, advanced activities of daily living (a-ADL/AADL) constitute a personal engagement in satisfying activities which are beyond what is needed to be independent and is therefore connected with volition, influenced by cultural and motivational factors (Reuben, Laliberte, Hiris & Mor, 1990).

ADL disability with loss of independence in the community represents a defining feature in the diagnosis of probable dementia (APA, 1994; McKhann et al., 1984; Tierney et al., 1988), whereas

according to Petersen et al. (1999) persons with MCI have largely preserved ADL. Thus, intact ADL is assumed to be a key differentiating feature distinguishing individuals with MCI from those with dementia (Gold, 2012; Jefferson et al., 2008; Petersen, 2011). Alternatively, on the grounds of previous studies which report a relationship between cognitive impairment and ADL disability in more advanced stages of AD and PDD (Barberger-Gateau & Fabrigoule, 1997; Castilla-Rilo et al., 2007; Christ et al., 2013; Giovannetti et al., 2012; Petersen, 2011), it could be assumed that a deterioration of ADL possibly already occurs at the very beginning of the cognitive losses. Evidence from several studies of the presence of ADL disability in individuals with MCI and PD-MCI emphasizes this thesis and the controversy regarding the construct of MCI due to the degree of functional impairment (Artero, Petersen, Touchon & Ritchie, 2006; Bangen et al., 2010; Broeders et al., 2013; Brown, Devanand, Liu & Caccappolo, 2011; De Vriendt et al., 2012; Farias et al., 2006; Gold, 2012; Hughes, Chang, Bilt, Snitz & Ganguli, 2012; Jefferson et al., 2008; Jekel et al., 2015; Leroi, McDonald, Pantula & Harbishettar, 2012; Perneczky et al., 2006a; Petersen et al., 2009; Reppermund et al., 2013; Rosenthal et al., 2010; Teng, Becker, Woo, Cummings &

Lu, 2010; Tuokko, Morris & Ebert, 2005; Yeh et al., 2011). In addition, according to Winblad et al. (2004) and their revised criteria of the MCI construct, both, cognitive as well as functional abilities need to be ascertained in the assessment of MCI. It is assumed that especially more complex ADL such as a-ADL and i-ADL are impaired in earlier stages of cognitive decline and an impairment of b-ADL only occurs later on as the disease progresses (Alzheimer's Association, 2011; Artero et al., 2006; Barberger-Gateau et al., 1999; Farias et al., 2006; Fields et al., 2010; Jefferson et al., 2008; Peres et al., 2006; Perneczky et al., 2006b). Thus, in particular a-ADL could be useful in detecting early functional decline or rather early-stage dementia since high cognitive functions are needed to perform such activities (Tuokko et al., 2005; Yeh et al., 2011). Alternatively, a-ADL are difficult to investigate owing to their dependence of cultural and gender influences and personal choices (Reuben et al., 1990). Thus, most studies focus on the assessment of i-ADL since they are also sensitive to cognitive decline in early-stage dementia and may therefore be important in screening for and diagnosing dementia (Barberger-Gateau et al., 2004; Cromwell, Eagar & Poulos, 2003; Peres et al., 2006).

According to Desai et al. (2004) more complex IADL disabilities are often

one of the first complaints to the person and/or caregivers. Furthermore, already the diagnosis of PD is associated with the decrease of ADL (Jasinska-Myga et al., 2012; Leroi et al., 2012; Young, Granic, Yu Chen, Haley & Edwards, 2010). It is believed that in addition to global cognitive decline pure motor abilities, such as rigidity or tremor, play an important role in IADL disability (Aarsland et al., 2007b; Gold, 2012; Leroi et al., 2012; Rosenthal et al., 2010). According to Aarsland et al. (2010) such motor symptoms predict more rapid cognitive decline and time to incident PDD. Moreover, Cahn et al. (1998) indicate that executive dysfunction, which is the main feature of PD (Litvan, Mohr, Williams, Gomez & Chase, 1991; Pillon, Dubois, Lhermitte & Agid, 1986), and not simple motor abilities represent an independent predictor of IADL abilities in PD. In addition, PDD patients exhibit significantly more functional impairment compared to persons with PD who are cognitive healthy (Giovannetti et al., 2012; Hobson & Meara, 2015). Thus, it may be useful to include measurements of ADL in the diagnostic process and investigate ADL disability both in preliminary stages of AD and PDD to ascertain whether they contribute to the early detection of dementia. Several studies already examined the role of functional impairment in patients with MCI, but until now there

are only very few studies about ADL disability and their role in cognitive decline concerning PD-MCI (Kulisevsky et al., 2013).

Previous studies have reported that functional impairment is associated with cognitive deficits in persons with MCI and PD-MCI, according to Desai et al. (2004) independent of demographics, lifestyle and medical factors (Anstey et al., 2013; Bangen et al., 2010; Perneczky et al., 2006b; Reppermund et al., 2011; Rosenthal et al., 2010) or rather that those with MCI and PD-MCI exhibit significantly more functional disability (on informant-reported ADL) than their cognitive normal counterparts (Aretouli & Brandt, 2010; Bangen et al., 2010; Broeders et al., 2013; De Vriendt et al., 2012; Farias et al., 2006; Jefferson et al., 2008; Leroi et al., 2012; Mariani et al., 2007; Perneczky et al., 2006a; Pirogovsky et al., 2013; Reppermund et al., 2013; Reppermund et al., 2011; Tabert et al., 2002; Tuokko et al., 2005; Yeh et al., 2011). This is also in line with studies that utilized objective measures of everyday function (Bangen et al., 2010; Pirogovsky et al., 2013; Reppermund et al., 2011). Moreover, according to Artero et al. (2006) twice as many individuals with MCI show increasing difficulties with at least one IADL as opposed to cognitively intact individuals. Further, Perneczky et al.

(2006a) found that both cognitive testing as well as informant-based interviews on ADL ability discriminated very well between MCI patients and healthy elderly. In addition, aMCI as well as PD-aMCI individuals show more ADL disability than people suffering (PD-)naMCI (Bangen et al., 2010; Farias et al., 2005; Luck et al., 2011; Reul, 2013; Teng et al., 2010; Wadley et al., 2007). According to the review of Gold (2012) and the study of Gure et al. (2013) functional abilities gets statistically worse from healthy older adults to individuals with MCI and finally to dementia, with moderate to large effect sizes. Thus, MCI may represent a functional status between the subtle decrements of aging and the more severe impairments in persons diagnosed as having dementia (Reppermund et al., 2013). Therefore, investigating differences concerning the extent of ADL disability in aging and MCI could contribute to better prognostication of the disease and earlier intervention (Aretouli & Brandt, 2010), which further suggests that it would not be useful distinguishing patients with MCI from those who are demented in regard to intact ADL (Perneczky et al., 2006a).

In addition, SCD may also be a risk factor of cognitive decline in patients from a memory clinic, because an association has been found between SCD and other factors accompanying the progress of

dementia, amongst other things, also with more impaired ADL, has been found (Clarnette, Almeida, Forstl, Paton & Martins, 2001; Montejo, Montenegro, Fernández & Maestú, 2012; Stewart, 2011). According to Waldorff et al. (2012) SCD may be an indication of vulnerability and together with ADL disability it may be associated with increased risk of dementia. Further according to Hong et al. (2014) in PD patients the presence of SCD and functional impairment were significant risk factors for incident MCI. But overall, there is a lack of studies concerning the role of ADL disability in individuals with SCD so far.

Furthermore, longitudinal studies are needed exploring the role of ADL disability and their impact on cognitive decline more accurately, because conclusions from cross-sectional investigations such as described above are limited (Gold, 2012). Longitudinal studies found that functional impairment represents a risk factor of cognitive decline (incident MCI) and a strong predictor of progression to dementia in individuals with MCI, even after controlling for possible confounding variables (Barberger-Gateau et al., 1993; Di Carlo et al., 2007; Fauth et al., 2013; Luck et al., 2011; Peres et al., 2006; Reppermund et al., 2013; Sikkes et al., 2011; Tabert et al., 2002). Thus, individuals with IADL disability at

baseline show a higher conversion rate and have a lower chance of "reversion" to normal cognition (Luck et al., 2011; Sikkes et al., 2011). In addition, Fauth et al. (2013) indicate that, after controlling for cognitive status, gender, age and depressive symptoms, subjects with IADL disability exhibit an 83% higher risk of developing dementia. Further MCI participants with functional impairment at baseline are at greater risk for dementia, exhibit more rapid functional decline and convert to dementia faster than those without ADL disability (Gold, 2012; Jekel et al., 2015; Luck et al., 2011; Peres et al., 2006; Purser, Fillenbaum, Pieper & Wallace, 2005). Moreover, regarding to subtypes of MCI, subjects with aMCI and IADL dysfunction are at greatest risk for the development of dementia and also in individuals suffering naMCI, those with impaired ADL have a higher conversion rate and a shorter time to incident dementia (Luck et al., 2011). In addition, Peres and colleagues (2006) found that also self-reported IADL disability was able to predict future dementia after two years, even for persons with normal performance on neuropsychological observations. These findings could be replicated by the four years follow-up investigation by Di Carlo et al. (2007). In a further examination of Peres et al. (2008) they indicate that, after co-varying for general function, education,

sex and age, difficulties in two or more self-reported IADL items significantly predicted risk of dementia ten years prior to the diagnose in subjects with MCI and cognitive normal ones. Further, Purser et al. (2005) examined 2,371 healthy elderly and 810 individuals with MCI over a period of 10 years and found that, based on self-reported IADL, MCI subjects with disability in their IADL exhibit a higher risk of developing dementia and appear to progress more quickly than those without disability, albeit their memory performance has deteriorated over the observation period. Thus, it is noteworthy that after controlling for demographic and clinical variables, there was no significant difference with regard to conversion rate between individuals with MCI and their cognitive normal counterparts, unless they also show IADL difficulties. Thus, not only cognitive (Alzheimer's Association, 2011; Elias et al., 2000; Snowdon et al., 1996), but also functional deficits may appear years before the diagnosis of dementia.

Looked at in another way, a recent meta-analysis of sixteen prospective studies from Hamer and Chida (2009) and the review of Rolland, Abellan van Kann and Vellas (2008) demonstrate that physically inactive individuals were at significantly increased risk of cognitive deficits and future dementia. Moreover,

aerobic exercise interventions showed modest improvement in cognition regarding to individuals with SCD and cognitive healthy elderly (Angevaren, Aufdemkampe, Verhaar, Aleman & Vanhees, 2008; Lautenschlager et al., 2008).

#### **1.4 Study overview – Aim of the study**

IADL disability may play an important role in detecting subjects who will convert to AD or PDD in earlier stages of the disease and thus they may be useful in the diagnostic process. As stated by Sikkes et al. (2011), longitudinal studies in memory clinics with higher prevalence rates of dementia are needed to examine the impact of IADL in detecting dementia. Therefore, this longitudinal cohort study uses data from an outpatient memory clinic and aims to investigate whether restrictions concerning IADL in precursors of dementia (SCD, naMCI, aMCI; PD-SCD, PD-naMCI and PD-aMCI) represent a risk factor and are therefore meaningful for the diagnostic process. Whereat, self-reported IADL were ascertained with the Bayer Activities of Daily Living Scale (B-ADL) (Erzigkeit & Lehfeld, 2010) and the diagnosis, amongst other things, through the Neuropsychological Test Battery Vienna (NTBV) (Lehrner, Maly, Gleiß, Auff & Dal-Bianco, 2007).

According to literature the expectations are the following:

- Subjects with MCI and PD will report significantly more IADL disability than individuals with SCD.
- MCI and PD patients will describe an increased deterioration over the course of study in IADL compared to subjects with SCD.
- Individuals with aMCI and naMCI will report significantly more IADL disability than people with SCD, in which patients with aMCI will describe the highest restrictions in IADL.
- Patients with aMCI and naMCI will report an increased deterioration over the course of study in IADL compared to subjects with SCD, in which patients with aMCI will deteriorate most in their self-reported IADL.
- Concerning patients with PD, no significant differences will be expected due to the small sample sizes, but it is assumed that individuals with PD-SCD will report the lowest and patients with PD-aMCI the highest difficulties in their IADL and that individuals with PD-aMCI will deteriorate most in their self-reported IADL.
- Converters to AD will describe significantly more IADL disability at baseline than Non-Converters and will have a greater deterioration in their self-reported IADL over the course of

study.

- Individuals who deteriorated over the course of the study with regard to their diagnosis will describe significantly more IADL disability at baseline and will report an increased deterioration over the course of study in IADL than people who remained stable.
- In subjects with PD, regarding to those who deteriorated or remained stable over the study period, the same will be assumed, but without significant differences.

## **2. Methods**

### **2.1 Procedure and Subjects**

The data for the present quasi-experimental longitudinal study were collected in a memory outpatient clinic and are part of a larger research project, the Vienna Conversion to Dementia Study (VCDS), from the Department of Neurology at the Medical University of Vienna. The study complies with the ethical principles of Helsinki's Declaration and was authorized by the Ethics Committee of the Medical University of Vienna. Furthermore, written informed consent for study participation was received from all patients. The patients were either self-referrals or were referred by the Department of Neurology for further examination of assumed and subjectively perceived cognitive deficits or were invited to participate in the course of



follow-up assessment. The average time span between baseline and follow-up investigation was nearly 33 months (SD = 15.8, ranging from 12 to 60 months).

Patients underwent screening tools, a complete neuropsychological examination (with a duration of about 45 – 60 minutes) and relevant self-assessment questionnaires in just one session and information about memory complaints, their medical history, regular medications and socio-demographic data (age, years of education and employment status) were procured, using the brief cognitive rating scale (Reisberg & Ferris, 1987). Furthermore, standard laboratory blood tests and psychometric tests and more often than not a computer tomography (CT) scan or a magnetic resonance imaging (MRI) scan were carried out.

Similar to prior studies, criteria for exclusion from the current study were as follows: (1) Cortical stroke, ascertained by neuroradiologic and clinical examination; (2) history of severe head injury; (3) medical conditions that interfere with normal cognition, including renal, cardiac, respiratory and hepatic disease; (4) Current psychiatric disorder based on International Classification of Diseases, tenth revision (ICD-10) (Dilling, Mombour & Schmidt, 2008), beyond mild depressive symptoms; (5) Age less than 50 years; and (6) presence of dementia according to

Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) (Saß, Wittchen, Zaudig & Houben, 2003).

The resulting total sample of  $N = 168$ , that came to the memory outpatient clinic, from Vienna, Lower Austria or Burgenland, included patients with SCD, MCI, PD-SCD and PD-MCI. The sample consisted of 90 women (53.6%) and 78 men (46.4%) between 50 and 88 years of age ( $M = 67.5$ ,  $SD = 9.1$ ). At baseline, the mean MMSE score was 28.1 ( $SD = 1.6$ ) and years of education ranged from 7 to 22 ( $M = 11.7$ ,  $SD = 3.6$ ). For measures including values of the Bayer Activities of Daily Living Scale (B-ADL) (Erzigkeit & Lehfeld, 2010) a baseline sample of  $N=162$  remained due to missing values. After allocation to the different groups of diagnosis with regard to the total sample of  $N = 168$ , sixty-nine (41.1%) subjects had SCD, 41 (24.4%) patients were diagnosed with aMCI, 31 (18.5%) individuals belonged to the group naMCI, 27 (16.1%) patients suffer PD of whom two (1.2%) subjects had PD-SCD, nine (5.4%) individuals were in the group PD-aMCI and 16 (9.5%) patients were diagnosed with PD-naMCI (see Table 1).

## **2.2 Measurement Instruments**

### **2.2.1 Screening procedures**

For an overview the Mini Mental Status Examination Test (MMSE) (Folstein, Folstein & McHugh, 1975), the

Clock Drawing Test of Sunderland, Hill, Mellow and Lawlor (1989), the “Wortschatztest” (WST) (Schmidt & Metzler, 1992) and the “Test zur Erfassung der Visuokonstruktion” (VVT) (Lehrner et al., 2015) were applied.

### **2.2.2 Neuropsychological Measurements – Objective cognitive performance**

The NTBv (Lehrner et al., 2007) was the main instrument for diagnosis. The initial use of the standardized, validated and normed NTBv detects dementia in clinical settings whilst the assessed cognitive function domains, with corresponding domain- and total z-scores across all tests described below, investigate a broad range of cognitive abilities regularly impaired in individuals with dementia and cognitive decline (Lehrner et al., 2007; Pusswald et al., 2013). Concerning the total population and individuals diagnosed as having dementia, Cronbach alpha ranges from 0.83 to 0.93 respectively from 0.87 to 0.89, which indicates a high internal consistency. For test-retest reliability correlation coefficients range from  $r = .86$  to  $.94$  respectively from  $r = .69$  to  $.90$  (Lehrner et al., 2007; Macher, 2013).

The neuropsychological test battery quantifies (1) Attention, (2) Language, (3) Memory, (4) Phonemic verbal fluency, (5) Interference, and (6) Planning and

nonverbal fluency. Following subtests were utilized to examine these domains:

(1) Attention: Alters-Konzentrations-Test (AKT) (Gatterer, 2008); Digit-symbol subtest of the German Wechsler Adult Intelligence Scale – Revised (WAIS-R) (Tewes, 1994); Symbol counting task from the Cerebral Insufficiency Test (C.I.) (Lehrl & Fischer, 1997); Trail Making Test version B (TMTB); score difference from the Trail Making Test version A (TMTA) and TMTB (Reitan, 1979).

(2) Language: Semantic Verbal Fluency Test (Goodglass & Kaplan, 1983); modified Boston Naming Test (BNT) (Morris et al., 1989).

(3) Memory: Verbal Selective Reminding Test (VSRT) (Lehrner et al., 2007).

(4) Phonemic verbal fluency - executive functioning: Phonemic Verbal Fluency Test (Goodglass & Kaplan, 1983).

(5) Interference - executive functioning: Stroop test from the Nürnberger Aging Inventory (NAI) (Oswald & Fleischmann, 1997); Interference subtest from the C.I. (Lehrl and Fischer, 1997).

(6) Planning and nonverbal fluency – executive functioning: TMTA (Reitan, 1979); Five-Point Test (Regard, Strauss & Knapp, 1982); Maze Test from the NAI (Oswald & Fleischmann, 1997).

### **2.2.3 The Bayer Activities of Daily Living Scale (B-ADL)**

The Bayer Activities of living Scale (B-ADL) (Erzigkeit & Lehfeld, 2010) assesses difficulties of more complex everyday activities owing to self-reported or informant-based judgements and is mainly developed for community dwelling subjects with mild cognitive impairment or mild-to-moderate dementia. It consists of 25 items with a ten-class scale from “never“ to “always“. The two introductory items concerning managing everyday activities and taking care of him or herself are intended as ‘warming-up’ questions, whereas items from 3 to 20 refer to difficulties in specific daily activities. Furthermore, items from 21 to 25 refer specifically to cognitive deficits. For evaluation the average score of all 25 items is computed. Higher scores mean greater impairment of ADL. According to Erzigkeit and Lehfeld (2010) the following interpretation is proposed: 1.0 to 2.0 - no difficulties; 2.1 to 5.0 - slight difficulties; 5.1 to 10.0 - significant difficulties in coping with everyday life activities. In addition, reliability ( $r = .98$ ) and validity with regard to the German version of the B-ADL are quite satisfactory (Erzigkeit & Lehfeld, 2010; Hindmarch, Lehfeld, de Jongh, & Erzigkeit, 1998).

### **2.3 Classification procedure**

The diagnosis was carried out using the NTBv and in consensus with other employees like neurologists or

neuropsychologists of the Department of Neurology. For the evaluation and comparability of individual test performance raw scores of each subtest were transformed into z-scores. These z-values were calculated depending on age, gender and education on a cognitive healthy control sample since there is evidence that these demographic variables interfere with cognitive variables (Chandler et al., 2005; Pusswald et al., 2013). Based on the current guidelines according to Petersen (2004, 2011), MCI was diagnosed with a standard deviation greater than -1.5 below age-, gender- and education-adjusted normal ranges in at least one subtest. As already mentioned above, aMCI was diagnosed as soon as the memory domain (z-score below -1.5) deemed to be impaired. Further, if no examined domain had a z-value greater than -1.5, participants were classified as having SCD since all subjects that came to the memory outpatient clinic complained about cognitive deterioration. Finally, at follow-up examination, dementia was diagnosed according to the criteria described in DSM-IV (Saß et al., 2003) respectively ICD-10 (Dilling et al., 2008) and in a consensus conference with neurologists. Diagnoses regarding PD-SCD, PD-MCI and PDD followed the same procedure.

## 2.4 Statistical Analysis

Statistical analyses were done using IBM SPSS statistics 22.0 for Windows. Descriptive statistics were utilized for sample characterization and demographic variables and neuropsychological data were described by means and standard deviations. Before, the main analyses conversion rates with regard to the diagnostic groups (SCD, naMCI, aMCI, AD; PD-SCD, PD-naMCI, PD-aMCI) were calculated using cross tabulations. Further, although the normal distribution cannot be assumed in some sub-samples, repeated-measure ANOVAs was performed for a portion of the main analyses under reference to the central limit theorem and the increased statistical power of this test compared to non-parametrical tests (Bortz & Döring, 2006; Field, 2009). Thus, for the main analyses, except for Step 3, which consists of 4 steps and is described in more detail below, repeated-measure ANOVAs was performed with groups of diagnoses as a between factor and time as a within factor, whereby test scores of the B-ADL acted as dependent variables and diagnostic groups as independent variable. In addition, pairwise comparisons were performed using Bonferroni-corrected post-hoc tests and effect sizes of partial eta-square ( $\eta^2p$ ) were calculated as well, in which according to Cohen (1988)  $\eta^2p = .01$

represents a small effect size,  $\eta^2p = .06$  a medium effect size and  $\eta^2p = .14$  a large effect size (Cohen, 1988). Moreover, in patients with PD and in calculations between Converts and Non-Converters (Step 3) the violation of normal distribution appeared exaggerated, as the group sizes are too small. For non-parametrical analyses and further analyses regarding to other variables of interest, one-way ANOVAs, Kruskal-Wallis tests, t-tests and Mann-Whitney tests were performed. Furthermore, a Receiver Operating Characteristic (ROC) curve was conducted to assess the predictive value of the B-ADL. The Area under the curve (AUC) represents an indicator of the prognostic utility of the B-ADL (Bortz & Döring, 2006), whereby an area of 1 indicates a perfect test and an area of .5 can be equated with random assignment (Weiß, 2013). The optimal cut-off score was calculated by selecting the point on the ROC curve that demonstrates the highest sensitivity and specificity, whereby sensitivity indicates the likelihood that subjects with AD are correctly classified as demented and specificity indicates the probability that non-demented individuals are correctly identified as healthy (Weiß, 2013). Additionally, positive predicted value (PPV) and negative predicted value (NPV) as well as positive likelihood ratio (LR+) and negative likelihood ratio

(LR-) were calculated (Weiß, 2013), whereby a  $LR^+ > 10$  reliably include an AD and a  $LR^- < 0.1$  reliably exclude the disease in question. Furthermore, a  $LR^+$  between 5 and 10 respectively a  $LR^-$  between .1 and .2 yield moderate changes in the pretest probability and a  $LR^+$  between 2 and 5 respectively a  $LR^-$  between .5 and .2 are hardly clinically relevant (Glenck, Pewsner & Bucher, 2001). Moreover, Spearman  $r$  correlations were carried out to detect associations between ADL and variables of interest in which  $r_s = .10$  represents a small effect size,  $r_s = .30$  a medium effect size and  $r_s = .50$  a large effect size (Cohen, 1988). Finally, the level of statistical significance was set to 0.05 across all statistical procedures.

### 3.4.1 Step 1

In Step 1 the question was investigated whether the self-reported IADL significantly differ between the diagnostic groups SCD, MCI and PD and if these significantly differ over the survey period with regard to the first diagnosis. Therefore, a 3x2-repeated-measure ANOVA was performed. Further, one-way ANOVAs respectively Kruskal-Wallis tests were used to look for differences in other interesting variables such as age, years of education, MMSE scores, interval between baseline and follow-up measures and WST-IQ.

### 3.4.2 Step 2

Step 2 focused on whether the self-reported IADL significantly differ between the diagnostic (sub-)groups SCD, naMCI and aMCI and if these significantly differ over the study period concerning the baseline diagnosis. Therefore a 3x2-repeated-measure ANOVA was conducted. Comparisons between PD patients and non-PD subjects were not sensible as the sample sizes in the diagnostic groups are too small and therefore also the conditions of normal distribution cannot be assumed. Concerning patients suffering PD, Kruskal-Wallis tests were performed separately with the baseline measures and the difference of the B-ADL scores to investigate differences in IADL disability across the diagnostic groups PD-SCD, PD-naMCI and PD-aMCI and over the course of study. Additionally, one-way ANOVAs respectively Kruskal-Wallis tests were used to look for differences with regard to other interesting variables.

### 3.4.3 Step 3

In Step 3 a Mann-Whitney test (U-Test) was performed concerning the baseline values of the B-ADL in individuals who converted to AD and those who are not to investigate if Converters already differ significantly from Non-Converters in their baseline measures of functional ability. Furthermore, a U-test with regard to the difference of the B-ADL

scores was used to examine whether these significantly differ over the course of study. Moreover, t-tests or U-tests were carried out to look for differences in other interesting variables.

#### 3.4.4 Step 4

Step 4 investigated whether the self-reported IADL significantly differ over the study period depending on whether the diagnosis has deteriorated or remained stable. Assignment to the two groups was based on the suggested course “SCD → naMCI → aMCI → AD” (Jessen et al., 2010). Therefore a 2x2 repeated-measure ANOVA was conducted. Concerning PD-patients U-tests were calculated with the baseline measures and the difference of B-ADL scores to look for differences in IADL disability across the diagnostic groups PD-SCD, PD-naMCI and PD-aMCI and over the course of study. In addition, t-tests or U-tests were used to examine differences in other interesting variables.

### 3. Results

#### 3.1 Conversion rates

Table 2 shows the conversion rates over all groups of diagnoses. It can be seen that from 69 patients with SCD on the baseline measure 39 (56.5 %) remained, 29 (42 %) went on to MCI [11 (15.9 %) to aMCI and 18 (26.1 %) to naMCI] and one patient (1.4 %) converted to AD. In patients with MCI as baseline diagnosis eleven (15.3 %) resumed to SCD at follow-

up. 54 (75 %) individuals remained unchanged with respect to their diagnosis and 7 (9.7 %) became demented, which corresponds to an OR of 7.3 [CI 0.9 to 61.2] for MCI compared to SCD. When we focus on aMCI and naMCI separately, in six (14.6 %) people diagnosis of aMCI improved to SCD and in five (16.1 %) patients the diagnosis changed from naMCI to SCD. Further 17 (41.5 %) remained aMCI and ten (32.3 %) remained naMCI. 13 (31.7 %) individuals changed from aMCI to naMCI and 14 (45.2%) from naMCI to aMCI. Finally, five (12.2 %) patients went on from aMCI to AD and two (6.5 %) from naMCI to AD, indicating an OR of 2.0 [CI 0.4 to 11.2] for aMCI vs. naMCI. Thus, in this study with one follow-up investigation a total of eight (5.7 %) subjects converted to AD.

Furthermore, from the patients with PD-SCD on the baseline measure two patients (100 %) went on to PD-MCI, one to PD-aMCI (50 %) and one to PD-naMCI (50 %). Concerning PD-MCI at baseline 23 (87.5 %) remained stable and two (12.5 %) improved to SCD. Further seven (77.8 %) were diagnosed with PD-aMCI at baseline and follow-up and two (22.2 %) changed from PD-aMCI to PD-naMCI. In people with PD-naMCI at baseline two (12.5 %) resumed to SCD at follow-up, four (25 %) had deteriorated to PD-aMCI and ten (62.5 %) remained stable. All in all, none of the

PD patients converted to PDD.

### 3.2 Main analyses

#### 3.2.1 Step 1

**Do self-reported IADL significantly differ between the diagnostic groups SCD, MCI and PD and do these differ significantly over the study period with regard to the first diagnosis?**

There is a significant main effect of diagnosis ( $F(2, 155) = 4.19, p < .005, \eta^2p = .051$ ) and a significant main effect of time ( $F(1, 155) = 6.69, p < .005, \eta^2p = .041$ ) but no interaction effect ( $F(2, 155) = 0.58, p = .560, \eta^2p = .007$ ). Post hoc analysis show, that subjects with MCI differ significantly in their reported IADL compared to individuals with SCD ( $p < .05$ ). Taking into account the mean values, individuals with MCI report significantly more IADL disability than subjects with SCD and people with MCI described a deterioration twice as high in their IADL when compared with the two other diagnostic groups. Further PD-patients actually described the highest average difficulties in IADL at baseline (Fig. 1.). Moreover MMSE scores ( $H(2) = 9.31, p < .05$ ), the interval between baseline and follow-up measures ( $H(2) = 10.83, p < .01$ ) and the WST-IQ ( $H(2) = 14.04, p < .01$ ) differ significantly with regard to the diagnostic groups. Table 1 shows the means and standard deviations for variables of interest

as well as for the dependent variable.

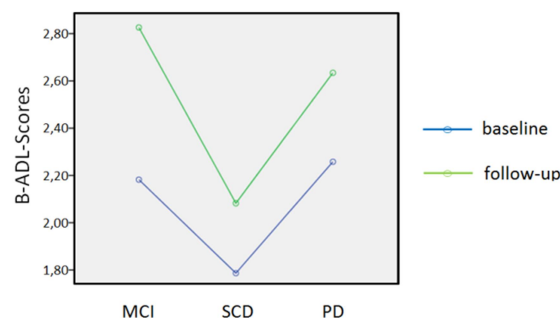


Fig. 1. B-ADL-Scores at baseline and follow-up across Step 1

#### 3.2.2 Step 2

**Do self-reported IADL differ significantly between the diagnostic groups SCD, naMCI and aMCI and do these differ significantly over the study period concerning the baseline diagnosis?**

There is a significant main effect of diagnostic subgroups ( $F(2, 131) = 4.11, p < .005, \eta^2p = .059$ ) and a significant main effect of time ( $F(1, 131) = 9.29, p < .001, \eta^2p = .066$ ) but no interaction effect ( $F(2, 131) = 0.58, p = .561, \eta^2p = .009$ ). Post hoc analysis show that subjects with aMCI differ significantly from those with SCD with regard to their reported IADL ( $p < .05$ ). Under consideration of the average scores, individuals with aMCI report significantly more IADL disability than subjects with SCD, in which there can be seen that the self-reported severity of IADL disability and the deterioration during the course of study increases in a stepwise manner from SCD to naMCI to

aMCI (Fig. 2.). Moreover years of education ( $H(2) = 7.11, p < .05$ ), MMSE scores ( $H(2) = 10.88, p < .01$ ), the interval between baseline and follow-up measures ( $H(2) = 6.41, p < .05$ ) and the WST-IQ ( $H(2) = 15.53, p < .01$ ) differ significantly with respect to the diagnostic groups. A description of means and standard deviations for variables of interest as well as for the dependent variable are shown in table 1.

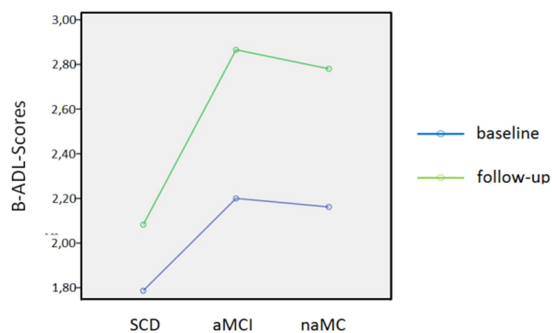


Fig. 2. B-ADL-Scores at baseline and follow-up across Step 2

### **Do self-reported IADL differ significantly across the diagnostic groups PD-SCD, PD-naMCI and PD-aMCI?**

Self-reported IADL did not differ significantly in any of the three diagnostic groups nor were there significant differences over the course of study. But in view of the mean values patients with PD-SCD described the lowest and PD-aMCI the highest disability in their IADL. Further, both PD-naMCI and PD-aMCI deteriorated over the study period with regard to their self-reported IADL (Fig. 3.). In addition, years of education ( $H(2) =$

$8.50, p < .05$ ) and MMSE scores ( $H(2) = 6.02, p < .05$ ) differ significantly regarding to the diagnostic groups. Table 1 shows the means and standard deviations for variables of interest as well as for the dependent variable.

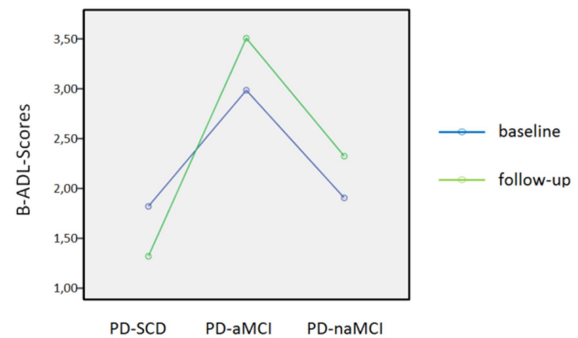


Fig. 3. B-ADL-Scores at baseline and follow-up across Step 2 (PD)

### **3.2.3 Step 3**

#### **Do Converters to AD and Non-Converters differ significantly in their self-reported baseline values of the B-ADL?**

Individuals who convert to AD differ significantly in their self-reported IADL at baseline in comparison to Non-Converters ( $U(8, 128) = 280.5, p < .05$ ) but did not significantly differ over the study period. Further, according to average scores Converters reported significantly higher IADL disability than Non-Converters and the deterioration during the course of study was nearly twice as high in Converters as in Non-Converters (Fig. 4.). Further, MMSE scores ( $U(8, 133) = 211.5, p < .01$ ) and the interval between baseline and follow-up measures ( $U(8, 133) = 307, p < .05$ ) differ significantly concerning the



diagnostic groups. A description of the means and standard deviations of baseline and follow-up characteristics concerning Converters and Non-Converters are shown in table 3.

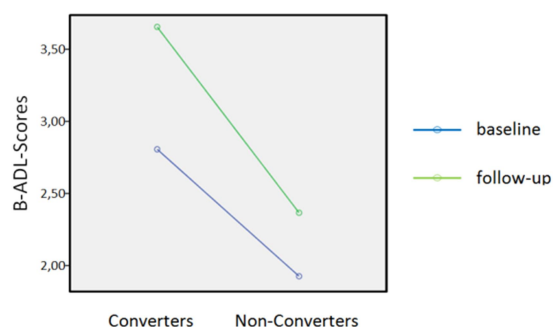


Fig. 4. B-ADL-Scores at baseline and follow-up across Step 3

### 3.2.4 Step 4

**Do self-reported IADL differ significantly over the study period depending on whether the diagnosis has deteriorated or remained stable in subjects with SCD, naMCI, aMCI and AD?**

There is a significant main group effect ( $F(1, 110) = 5.58, p < .005, \eta^2p = .048$ ) and a significant main effect of time ( $F(1, 110) = 7.02, p < .001, \eta^2p = .060$ ) but no interaction effect ( $F(1, 110) = 1.75, p = .188, \eta^2p = .016$ ). Taking into account the mean values, individuals which have deteriorated in their diagnoses over the study period report significantly poorer IADL at baseline and a deterioration in their IADL ability more than twice as high than those who have remained stable (Fig. 5.). Moreover, MMSE scores ( $U(49, 62) = 1176, p < .01$ ) differ significantly with

regard to the diagnostic groups. Table 4 shows the means and standard deviations of baseline and follow-up characteristics.

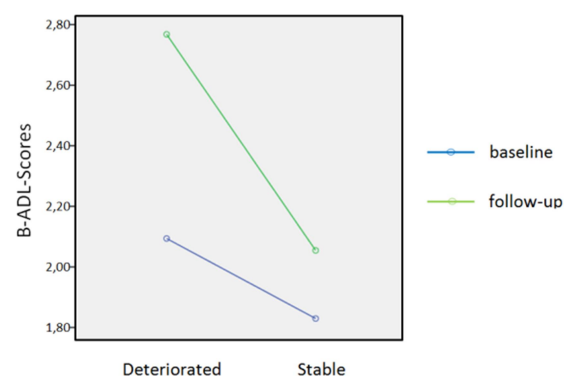


Fig. 5. B-ADL-Scores at baseline and follow-up across Step 4

**Do self-reported IADL differ significantly over the study period depending on whether the diagnosis has deteriorated or remained stable in patients with PD-SCD, PD-naMCI and PD-aMCI?**

Self-reported IADL did not differ significantly in people who deteriorated in their diagnoses and those who have remained stable nor did they describe significant differences over the course of study. In view of the mean values, both patients who deteriorated in their diagnoses and those who remained stable described higher IADL disability at follow-up measures. But people who remained stable in their diagnoses reported more IADL difficulties at baseline and described an increased deterioration over the course of study (Fig. 6.). Table 5 shows the means and standard deviations for variables of

interest as well as for the dependent variable.

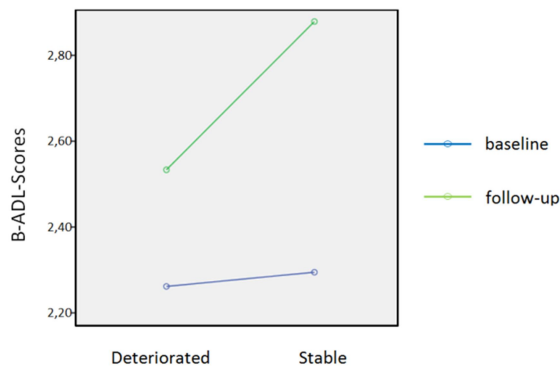


Fig. 6. B-ADL-Scores at baseline and follow-up across Step 4 (PD)

### 3.3 ROC-Analysis

A Receiver Operating Characteristic (ROC) curve was conducted to assess the predictive value of the B-ADL. The result of the ROC-analysis (see Fig. 7.) revealed an AUC of .726, 95% CI [.52 to .93] with a standard error of .105 ( $p = .032$ ).

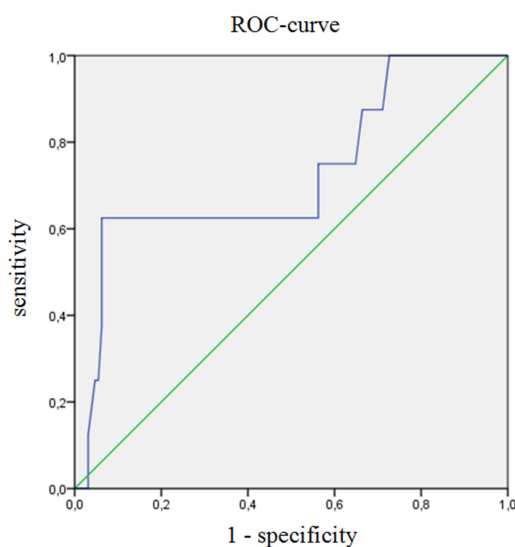


Fig. 7. ROC – curve analysis concerning B-ADL

The optimal B-ADL cut-off score was 3.40 with a Youden – Index of .56. Moreover, a sensitivity of .63, 95% CI [.31 to .86] and a specificity of .94, 95% CI [.88

to .97] were obtained. A list of sensitivity and specificity with regard to different B-ADL scores are shown in table 6. Furthermore, concerning the cut-off score of 3.40, a PPV of .38, 95% CI [.17 to .65] and a NPV of .98, 95% CI [.93 to .99] were found. Additionally, a LR+ of 9.92, 95% CI [4.19 to 23.0] and a LR- of .40, 95% CI [.16 to .98] were obtained (see Fig.8.).

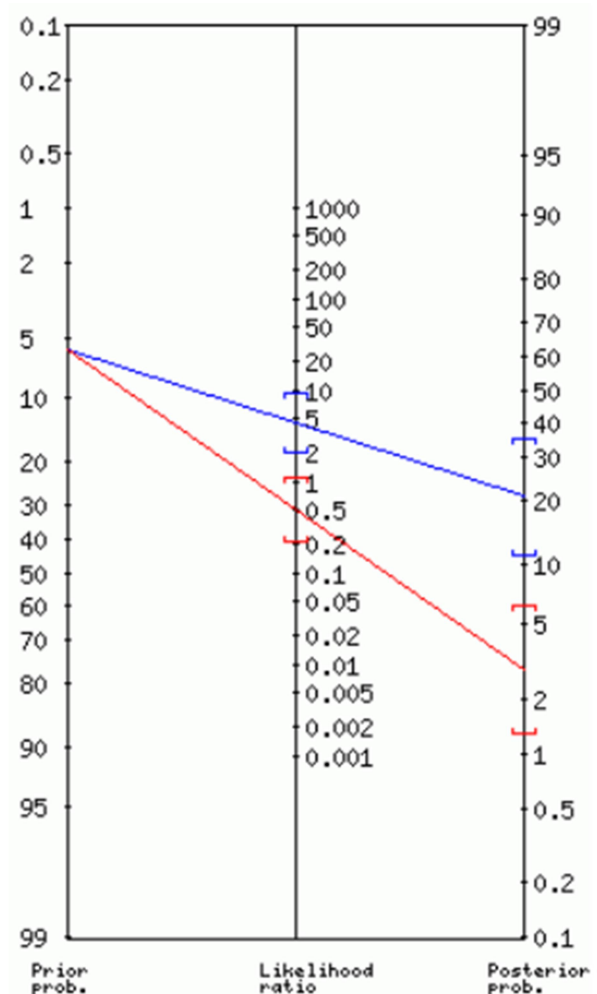


Fig. 8. Nomogram for interpreting diagnostic test results (LR) of B-ADL

### 3.4 Correlations between B-ADL-Scores and variables of interest

All correlations between B-ADL scores and variables of interest as well as

correlations between those in sub-samples of the present study are shown in table 7. There were no significant correlations between self-reported IADL and the age of the subjects, MMSE scores, and IQ measured by the WST. Further years of education only correlates significantly with self-reported IADL in the PD (total) group ( $r_s = -.40, p < .01$ ) and the interval between baseline and follow-up measures only correlates with those in regard to individuals with aMCI ( $r_s = -.42, p < .01$ ). Moreover, there is a correlation between the VSRT sub-test and the B-ADL scores in the MCI group ( $r_s = -.27, p < .05$ ) and for the total sample ( $r_s = -.21, p < .01$ ).

#### 4. Discussion

In the present quasi-experimental longitudinal study subjects who came to an outpatient memory clinic to seek help for possible cognitive deficits were investigated concerning differences in their ability to perform everyday activities in view of differences in objective cognitive impairment, with the major objective to draw conclusions about the meaningfulness of evaluating ADL disability in detecting AD and PDD. After measuring the objective cognitive deficits through the Neuropsychological Test Battery Vienna (NTBV) (Lehrner et al., 2007), individuals were diagnosed with SCD, na-MCI and a-MCI respectively PD-SCD, PD-naMCI and PD-aMCI. With

regard to these supposed precursors of dementia the differences in self-reported IADL, measured by the Bayer Activities of Daily Living Scale (B-ADL) (Erzigkeit & Lehfeld, 2010), were examined.

##### 4.1 Conversion rates

In this clinical study 5.7% of the total sample converted to AD during the investigation period, whereby 1.4% converted from SCD to AD and 9.7% from MCI to AD. According to OR subjects with MCI exhibit a 7.3 times higher risk of developing AD compared to individuals with SCD. Furthermore, the conversion rate of approximately 8 to 10% from MCI to AD, which was reported by Mitchell and Shiri-Feshki (2009), Petersen et al. (1999) and other researchers could be expected due to the clinical setting of this study which consequently consisted of persons seeking help for possible cognitive decline. Moreover, with respect to the subtypes of MCI, the conversion rate to AD is almost twice as high in subjects with aMCI (12.2 %) as in those with naMCI (6.5 %). This finding is also in line with previous studies (Busse et al., 2006; Fischer et al., 2007; Luck et al., 2011; Mitchell & Shiri-Feshki, 2009). In addition, 15.9% converted from SCD to aMCI and 26.1% to naMCI. Thus, the conversion rates from SCD to the subtypes of MCI and from SCD, naMCI and aMCI to AD replicated the trend “SCD  $\rightarrow$  naMCI  $\rightarrow$  aMCI” for the risk of

developing AD, which was reported by Jessen et al. (2010). Additionally, 45.2% changed in their diagnoses from naMCI to aMCI, whereas alternatively also 31.7% changed from aMCI to naMCI. This in turn suggests, that the course described by Jessen and colleagues (2010) isn't very stable and possibly a further differentiation of MCI subtypes would be needed, such as in single and multiple domain as supposed by Winblad et al. (2004). On the other hand the majority (75%) of individuals with MCI remained unchanged in their diagnoses. Thus, the sample sizes of individuals who changed within the subtypes of MCI were quite small. Another finding that indorses a further differentiation respectively a revision of the MCI construct is that 15.3% of individuals with MCI, with nearly the same percentages of aMCI and naMCI, resumed to SCD, which is in line with previous studies (Diniz, Nunes, Yassuda & Forlenza, 2009; Palmer, Fratiglioni & Winblad, 2003). Concerning patients with PD, none of them converted to PDD during the study period. This is inconsistent with results from earlier studies, which indicate an ACR of around 11% to 14%. This discrepancy might probably have resulted due to the small sample size of PD patients in the present study and therefore further interpretation concerning conversion rates in subsamples of PD does not make much

sense.

## 4.2 Main analyses

As expected, regarding to the main analyses, subjects with MCI at baseline reported significantly more IADL disability than those with SCD and people with MCI described a significant deterioration, twice as high, in their IADL when compared to individuals with SCD and PD. Further, although those with PD reported the highest restrictions of IADL, patients with PD did not significantly differ from subjects with SCD at baseline. This could be attributed to the small group size of PD patients compared to individuals with SCD and MCI. Moreover, the deterioration over the course of the study of self-reported IADL in subjects with PD barely differ from those with SCD.

Furthermore, as expected concerning SCD and the subtypes of MCI, individuals with aMCI described significantly more difficulties in their IADL than subjects with SCD, but contrary to expectation, naMCI did not. There was also a significant deterioration over the study period and it can be seen that also the self-reported severity of IADL disability and the deterioration during the course of study increased in a stepwise manner from SCD to naMCI to aMCI. These results further emphasize the trend along the continuum assumed by Jessen et al. (2010). In PD-

SCD and the subtypes of PD-MCI there were no significant outcomes, which were expected since the sub-samples are very small. What can be said is that individuals with PD-aMCI described higher IADL disability than those with PD-naMCI and that both deteriorated in their self-reported IADL over the study period. Subjects with PD-SCD barely differ from those with naMCI and also the expectation that people with PD-SCD describe the lowest and individuals with PD-aMCI the highest deterioration over the course of study is not consistent with the results of the present study.

As expected, according to a further investigation comparing self-reported baseline IADL in subjects who converted to AD with those who did not, Converters described significantly more restrictions in their IADL at baseline than Non-Converters. Both Converters and Non-Converters described deterioration in their IADL, in which the deterioration was twice as high in Converters as in Non-Converters. It can be assumed that the main effect of time was not significant due to the small group size of subjects who converted to AD ( $n = 8$ ).

In addition, as expected, subjects with SCD, naMCI, aMCI and AD, who deteriorated in their diagnoses over the study period compared to those who remained stable reported significantly

poorer IADL at baseline. Further, there was a significant time effect, in which subjects who deteriorated in their diagnoses described deterioration in their IADL ability more than twice as high as those who remained stable. As expected due to the small and unequal subgroups concerning people with PD-SCD, PD-naMCI and PD-aMCI, self-reported IADL did not differ significantly in subjects who deteriorated in their diagnoses and those who remained stable nor did they describe significant differences over the course of study. Further, the results of patients with PD show the exact opposite of what was initially expected. People who remained stable reported more restrictions in their IADL at baseline and described an increased deterioration over the study period compared to those who deteriorated regarding to their diagnoses.

### 4.3 Conclusion

The evidence from this study suggests that functional disability gets worse from SCD to naMCI to aMCI and finally to AD and therefore, it is able to discriminate between precursors of dementia and AD. Further, greater impairment concerning the ability to perform everyday activities at baseline is accompanied by more rapid functional decline and a higher risk for developing AD. Hence, functional disability represents an important risk factor of cognitive

decline (incident MCI) and progression to AD and seems to be a useful addition to the diagnostic process in a memory clinic setting. These assumptions are in line with the literature mentioned above. But it also must be said that effect sizes are small to moderate. Thus, it is important to bear in mind that both, the genesis of AD and disability in ADL represent multidimensional constructs, illustrated by the disablement process model by Barberger-Gateau, Fabrigoule, Amieva, Helmer and Dartigues (2002) (Leveille, Fried, McMullen & Guralnik, 2004; Verbrugge & Jette, 1994). According to the present study functional disability seems to be associated with cognitive deficits since ADL gets worse when cognitive abilities deteriorate. Further, MMSE scores, years of education, the interval between baseline and follow-up measures and the WST-IQ differed significantly with respect to the diagnostic groups. But both, demographic variables as well as other variables like the interval between baseline and follow-up measures, the WST-IQ and MMSE scores do not seem to relevantly influence self-reported restrictions in functional abilities. Moreover, there is a slight relationship between ADL disability and memory impairment, but conclusions about causality cannot be drawn. Additionally, also concerning patients with PD no

conclusions about the clinical value of functional disability in detecting dementia can be made due to the small sample size and the lack of subjects with PDD.

#### **4.4 Strengths and limitations**

The present study has the following strengths. Regarding to the inclusion of subjects with SCD a yet neglected research field was investigated. In addition, the latest definition of SCD by Jessen et al. (2014) was applied for the classification of individuals who report cognitive complaints. Moreover, the examined subjects were diagnosed using the NTBv that has a respectable discrimination power in detecting AD. Additionally, to my knowledge there was no longitudinal study investigating differences in self-reported IADL concerning the diagnostic groups SCD, naMCI and aMCI respectively PD-SCD, PD-naMCI and PD-aMCI until now. Moreover, a ROC-analysis was performed to evaluate the predictive power of the B-ADL assessment. When 3.40 was utilized as cut-off score, 62.5% of subjects with AD were correctly classified as demented and 93.8% were classified correctly as non-demented. Consequently, the false positive rate was 37.5% and the false negative rate was 6.2%. Based on the overall calculations of the ROC-analysis it can be concluded that the B-ADL score with regard to the present study constitutes a quite applicable method, however, there

is room for improvement.

Furthermore, this study also has some limitations. As frequently reported, the sample of patients with PD was quite small. Moreover, the differences in the time span between baseline and follow-up measures with regard to the investigated individuals could have influenced the conversion rates as well as other evaluations. It also must be mentioned that there was no information about cognitive or physical training or medication treatments that could have had an impact on cognitive and/or physical performance. Finally, the sample of the present study is very specific and thus results may not be generalizable to the general population. A further limitation could be that functional disability was assessed by self-reports of the affected. But it is also possible that the persons concerned themselves are sensitive for early restrictions in their abilities to perform everyday activities that relatives do not perceive so far and performance-based measures could not capture.

#### **4.5 Recommendations for future research**

Further studies should use multiple measures to investigate similarities and discrepancies between different measurement strategies of difficulties in ADL, since all of these strategies exhibit some advantages and disadvantages (Reppermund et al., 2013). Moreover, for

future research it would be useful to examine which specific ADL are impaired in early stages of AD/PDD (Gold, 2012) and investigate these ADL with regard to the further subdivision of aMCI and naMCI in single and multiple domain as supposed by Winblad et al. (2004). Further, since numerous potential risk factors, that are most likely involved in the development of AD and PDD, have already been detected, it would be necessary to consider them in interaction, and under consideration of individual variations over time, to develop uniform procedures, defining criteria, measurement instruments and questionnaires for better comparison of study outcomes and thus to tackle the challenge to identify a possible early dementia and ensure early interventions and medications.

#### **5.5 Summary**

To sum up, greater impairment in functional abilities at baseline is accompanied by more rapid functional decline and a higher risk for developing AD. Thus, functional disability represents an important risk factor of cognitive decline (incident MCI) and progression to AD and seems to be a useful addition to the diagnostic process in a memory clinic setting. However, further research is needed to encompass the multi-system of functional impairment and its impact on cognitive decline.

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Table 1. Baseline characteristics for diagnostic sub-groups (N = 168)

	Total (N=168)	SCD (n=69)	naMCI (n=31)	aMCI (n=41)	PD-SCD (n=2)	PD-naMCI (n=16)	PD-aMCI (n=9)
Female (n/%)	90/ 53.6	46/ 27.4	15/ 8.9	19/ 11.3	0/ 0.0	6/ 3.6	4/ 2.4
Age (years)	67.5/ 9.1	66.1/ 9.5	69.7/ 9.2	68.2/ 9.2	70.5/ 2.1	68.1/ 7.2	65.2/ 7.8
Education (years)	11.8/ 3.6	12.5/ 3.7	10.5/ 2.8	11.7/ 3.8	15.5/ 3.5	11.9/ 3.1	9.1/ 2.0
Intervall (months)	33.0/ 15.8	37.2/ 15.4	35.0/ 16.9	29.9/ 16.6	29.5/ 6.4	21.4/ 4.9	29.0/ 14.0
MMSE	28.1/ 1.6	28.5/ 1.3	27.4/ 1.8	27.9/ 1.4	28.5/ 0.7	28.6/ 1.3	26.4/ 2.4
WST	109.7/ 12.3 <sup>1</sup>	113.9/ 10.9	104.2/ 12.0 <sup>2</sup>	108.7/ 12.3	116.5/ 17.7	109.4/ 10.6	98.4/ 12.8 <sup>3</sup>
B-ADL	2.0/ 1.1 <sup>4</sup>	1.8/ 0.7	2.2/ 0.9 <sup>5</sup>	2.3/ 1.3 <sup>6</sup>	1.8/ 0.8	1.9/ 1.2 <sup>7</sup>	2.9/ 1.6

Note: variables are presented as mean & standard deviation; SCD, subjective cognitive decline; naMCI, nonamnesic mild cognitive impairment; aMCI, amnesic mild cognitive impairment; PD-SCD, Parkinson disease- subjective cognitive decline; PD-naMCI, Parkinson disease- nonamnesic mild cognitive impairment; PD-aMCI, Parkinson disease- amnesic mild cognitive impairment; MMSE, Mini Mental State Examination; WST, Wortschatztest; B-ADL, Bayer Activities of living Scale; WST <sup>1</sup>n=166 <sup>2</sup>n=30 <sup>3</sup>n=8; B-ADL <sup>4</sup>n=162 <sup>5</sup>n=30 <sup>6</sup>n=37 <sup>7</sup>n=15.

Note: SCD, subjective cognitive decline; naMCI, nonamnesic mild cognitive impairment; aMCI, amnesic mild cognitive impairment; AD, Alzheimer's disease, PD-SCD, Parkinson disease- subjective cognitive decline; PD-naMCI, Parkinson disease- nonamnesic mild cognitive impairment; PD-aMCI, Parkinson disease- amnesic mild cognitive impairment; no patients with PDD, Parkinson disease dementia.

Table 3. Characteristics of the Converters and Non-Converters (N = 141)

	Converters (n= 8)		Non-Converters (n= 133)	
	baseline	follow-up	baseline	follow-up
Female (n/%)	3/ 2.1	-	77/ 54.6	-
Age (years)	69.1/ 9.6	71.1/ 9.5	67.4/ 9.4	70.4/ 9.3
Education (years)	10.5/ 3.8	-	11.9/ 3.6	-
Intervall (months)	-	23.3/ 15.4	-	35.3 /16.1
MMSE	25.9/ 2.2	25.0/ 1.6	28.2/ 1.4	28.0/ 1.5
WST	107.4/ 14.2	103.3/ 11.3 <sup>1</sup>	110.5/ 12.0 <sup>2</sup>	108.2/ 18.2 <sup>3</sup>
B-ADL	2.8/ 1.1	3.7/ 2.7	2.0/ 0.9 <sup>4</sup>	2.3/ 1.8 <sup>5</sup>

Note: variables are presented as mean & standard deviation; MMSE, Mini Mental State Examination; WST, Wortschatztest; B-ADL, Bayer Activities of living Scale; WST <sup>1</sup>n=6 <sup>2</sup>n=132 <sup>3</sup>n=128; B-ADL <sup>4</sup>n=128 <sup>5</sup>n=131.

Table 4. Characteristics of the Sample - deteriorated and stable in SCD, naMCI, aMCI and AD (N = 117)

	Deteriorated (n = 51)		Stable (n = 66)	
	baseline	follow-up	baseline	follow-up
Female (n/%)	25/ 21.4	-	40/ 34.2	-
Age (years)	68.7/ 9.7	71.8/ 9.5	66.7/ 9.3	69.5/ 9.2
Education (years)	11.9/ 3.4	-	12.0/ 3.7	-
Intervall (months)	-	37.1/ 16.8	-	33.6/ 15.5
MMSE	27.6/ 1.8	27.7/ 1.8	28.5/ 1.2	27.9/ 1.6
WST	111.9/ 12.3	109.2/ 19.6 <sup>1</sup>	110.5/ 11.7 <sup>2</sup>	108.0/ 18.5 <sup>3</sup>
B-ADL	2.1/ 0.9 <sup>4</sup>	2.7/ 2.2	1.9/ 0.9 <sup>5</sup>	2.0/ 1.4 <sup>5</sup>

Note: variables are presented as mean & standard deviation; SCD, subjective cognitive decline; naMCI, nonamnesic mild cognitive impairment; aMCI, amnesic mild cognitive impairment; AD, Alzheimer's disease; MMSE, Mini Mental State Examination; WST, Wortschatztest; B-ADL, Bayer Activities of living Scale; WST <sup>1</sup>n=49 <sup>2</sup>n=65 <sup>3</sup>n=62; B-ADL <sup>4</sup>n=50 <sup>5</sup>n=64.

Table 5. Characteristics of the Sample - deteriorated and stable in PD-SCD, PD-naMCI and PD- aMCI (N = 23)

	Deteriorated (n = 6)		Stable (n = 17)	
	baseline	follow-up	baseline	follow-up
Female (n/%)	1/ 4.3	-	6/ 26.1	-
Age (years)	71.3/ 3.6	73.3/ 3.7	66.1/ 8.4	68.2/ 8.9
Education (years)	13.0/ 4.2	-	10.8/ 3.0	-
Intervall (months)	-	23.7/ 6.4	-	25.2/ 11.3
MMSE	27.8/ 1.6	27.2/ 1.7	28.1/ 1.9	28.1/ 1.4
WST	111.7/ 10.8	109.3/ 12.9	103.8/ 13.7 <sup>1</sup>	100.5/ 10.1 <sup>2</sup>
B-ADL	2.3/ 1.7	2.5/ 1.8	2.3/ 1.4 <sup>3</sup>	2.9/ 2.3 <sup>3</sup>

Note: variables are presented as mean & standard deviation; PD-SCD, Parkinson disease- subjective cognitive decline; PD-naMCI, Parkinson disease- nonamnesic mild cognitive impairment; PD-aMCI, Parkinson disease- amnesic mild cognitive impairment; MMSE, Mini Mental State Examination; WST, Wortschatztest; B-ADL, Bayer Activities of living Scale; WST <sup>1</sup>n=16 <sup>2</sup>n=15; B-ADL <sup>3</sup>n=16.

Table 6. Cut-off points and diagnostic validity of B-ADL

Cut off point	Sensitivity	Specificity	Youden Index
1,70	,625	0,516	0,141
1,74	,625	0,523	0,148
1,78	,625	0,547	0,172
1,84	,625	0,562	0,187
1,90	,625	0,578	0,203
1,94	,625	0,602	0,227
2,00	,625	0,609	0,234
2,06	,625	0,617	0,242
2,10	,625	0,625	0,250
2,13	,625	0,641	0,266
2,15	,625	0,648	0,273
2,20	,625	0,664	0,289
2,26	,625	0,687	0,312
2,30	,625	0,695	0,320
2,33	,625	0,703	0,328
2,35	,625	0,711	0,336
2,36	,625	0,719	0,344
2,39	,625	0,750	0,375
2,43	,625	0,758	0,383
2,45	,625	0,773	0,398
2,47	,625	0,781	0,406
2,50	,625	0,789	0,414
2,54	,625	0,805	0,430
2,62	,625	0,812	0,437
2,70	,625	0,836	0,461
2,73	,625	0,844	0,469
2,79	,625	0,852	0,477
2,85	,625	0,859	0,484
2,87	,625	0,867	0,492
2,90	,625	0,875	0,500
2,94	,625	0,883	0,508
3,00	,625	0,891	0,516
3,06	,625	0,906	0,531
3,14	,625	0,914	0,539
3,28	,625	0,922	0,547
<b><u>3,40</u></b>	<b><u>,625</u></b>	<b><u>0,937</u></b>	<b><u>0,562</u></b>
3,43	,500	0,937	0,437
3,46	,375	0,937	0,312
3,52	,250	0,945	0,195
3,62	,250	0,953	0,203
3,86	,125	0,969	0,094
4,10	,000	0,969	-0,031
5,20	,000	0,984	-0,016

Table 7. Spearman Correlations ( $r_s$ ) between baseline B-ADL-Scores and variables of interest

	age	N	education	N	intervall	N	MMSE	N	VSRT-DR	N	WST	N
SCD	-.003	69	-.149	69	.137	69	.018	69	.037	69	-.034	69
MCI	-.061	67	.110	67	-.230	67	-.081	67	-.272*	67	.011	66
PD (total)	.048	26	-.396**	26	-.095	26	-.252	26	-.325	26	.017	25
naMCI	.111	30	-.151	30	-.026	30	-.049	30	-.356	30	.005	29
aMCI	-.171	37	.283	37	-.423**	37	-.152	37	-.152	37	.005	37
PD-SCD <sup>1</sup>	1	2	1	2	1	2	1	2	-1	2	1	2
PD-naMCI	.111	15	-.317	15	-.121	15	.084	15	-.433	15	-.119	15
PD-aMCI	-.251	9	-.299	9	-.268	9	-.332	9	-.025	9	.383	8
Converters	-.524	8	.627	8	-.238	8	-.307	8	-.315	8	-.048	8
Non-Converters	-.009	128	-.047	128	-.059	128	-.018	128	-.142	128	-.047	127
Deteriorated	-.145	50	-.150	50	-.178	50	-.210	50	-.198	50	-.105	50
Stable	.093	64	-.081	64	-.054	64	.097	64	-.232	64	-.080	63
total	-.030	162	-.093	162	-.098	162	-.102	162	-.211**	162	-.035	160
total (SCD/ MCI)	-.029	136	-.028	136	-.094	136	-.067	136	-.193*	136	-.053	135

Note: SCD, subjective cognitive decline; naMCI, nonamnesic mild cognitive impairment; aMCI, amnesic mild cognitive impairment; PD-SCD, Parkinson disease-subjective cognitive decline; PD-naMCI, Parkinson disease- nonamnesic mild cognitive impairment; PD-aMCI, Parkinson disease- amnesic mild cognitive impairment; MMSE, Mini Mental State Examination; VSRT-DR, Verbal Selective Reminding Test-Delayed Recall; WST, Wortschatztest; <sup>1</sup>sample size only two subjects, interpreted with caution; .10 small, .30 moderate, .50 large effect size; \*  $p < .05$ . \*\*  $p < .01$ . (uncorrected  $p$ ).

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## Curriculum Vitae

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### Schulbildung

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Seit Oktober 2009	Psychologiestudium an der Universität Wien
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2004-2000	Regionalhauptschule Dobersberg
2000-1996	Volkschule Dobersberg

### Praktische Erfahrungen

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Oktober 2013-Mai 2014	Diagnostik in der Neurologie im AKH Wien im Rahmen meiner Diplomarbeit
September 2013	Praktikum im Bereich Klinische- und Gesundheitspsychologie im Landeskrankenhaus Waidhofen/Thaya
Juli-August 2013	6-Wochen Praktikum im psychosomatischen Zentrum Waldviertel in Eggenburg
Juli-August 2012	6-Wochen Pflichtpraktikum im Landesjugendheim Allentsteig im Ausmaß von 240h
Juli 2011	Praktikum in der Tagesstätte Zuversicht in Heidenreichstein
5. Februar 2009	Schnuppertag im Bereich Sozialarbeit und Psychiatrie im Landeskrankenhaus Waidhofen/Thaya
Juni-August 2007	3-monatiges Praktikum im Bereich Küche und Service
5-6 April 2007	Schnuppertage in der Physiotherapie im UKH Meidling

### Bisherige Berufstätigkeit

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Seit Mai 2011

geringfügige Tätigkeit als Betreuerin im Jugendzentrum  
Zwettl (JUZZ)

### Technische Kenntnisse

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Basisausbildung in Form des ECDL

- Modul 1: Grundlagen der Informationstechnologie
- Modul 2: Betriebssystem
- Modul 3: Textverarbeitung
- Modul 4: Tabellenkalkulation
- Modul 5: Datenbank
- Modul 6: Präsentation
- Modul 7: Internet

Andere:

- Macromedia Dreamweaver MX
- Adobe Photoshop 7.0
- Adobe InDesign 2.0
- Macromedia Flash 8
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### Fremdsprachen

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Englisch

Französisch